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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,720	01/17/2006	Haruo Imawaka	Q92718	1473
65565	7590	09/13/2007		
SUGHRUE-265550			EXAMINER	
2100 PENNSYLVANIA AVE. NW			ZUCKER, PAUL A	
WASHINGTON, DC 20037-3213				
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			09/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,720	Applicant(s) IMAWAKA ET AL.	
	Examiner Paul A. Zucker	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/17/06, 10/20/06</u> | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Specification

1. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 twice recites the limitation "curative" in line 10. Since there are no known cures for the recited disease states it is unclear what Applicants' intend to claim. Claim 17 is therefore rendered indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 11-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of some neurodegenerative disorders, does not reasonably provide enablement for prevention of any disorder or

treatment of disorders such as brain cancer or Down's Syndrome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

These factors include, but are not limited to:

- a. the breadth of the claims: In the instant case the claims are extremely broad encompassing compositions and methods for the prevention of any form of neurodegenerative condition including brain cancer in all its various forms, Down's disease or syndrome, Creutzfeld-Jacob disease, Huntington's disease, etc.
- b. the nature of the invention: The instantly claimed invention involves influencing astrocytes in the brain. While this may, in principle, have a therapeutic consequence, it is far from clear that demonstration of an *in vitro* effect will result in an *in vivo* effect. This especially true given the broad range of disease states recited, Brain cancer, for example, encompasses a large number of conditions each with its own characteristics.
- c. the state of the prior art: the state of the prior art is such that many of the disease states recited such as brain cancer in all its various forms, Down's disease or syndrome, Creutzfeld-Jacob disease, Huntington's disease, etc,

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- have no known treatment and no known method of prevention by pharmaceutical means. For example, there is no pharmaceutical method for the prevention of Down's syndrome, which is a genetic disorder.
- e. the amount of direction provided by the inventor: The inventor provide no direction for the use of the compounds of the invention for the treatment of any disease state.
- f. the existence of working examples: The only working examples provided are directed to the content of S100 β in astrocyte cells in culture. No examples of treatment of disease states is provided

Based upon the analysis above, the Examiner concludes that undue experimentation is required to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 4- 6 and 8-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Rettenmeier et al (Drug Metabolism and Disposition, Metabolic Fate of Valproic Acid in the Rhesus Monkey, 1986, 14(4), pages 443-453). Rettenmeier discloses (Page 452, Figure 7 and page 451, paragraph bridging columns 1 and 2 and 1st full

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paragraph, column 2) the valproic acid metabolites **9-12** and **15** all of which are compounds with $m=0$ as instantly claimed. The compounds are presumably in racemic form and are in aqueous solution. The composition claims are therefore considered to be anticipated since the intended use of a composition is not considered to be further limitative. Rettenmeier therefore anticipates claims 1, 4- 6 and 8-16.

5. Claims 1, 9, 11-15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohuchida et al (US 6,201,021 03-2001). Ohuchida discloses (Abstract) compounds useful for the treatment of neurodegenerative disease such as Alzheimer's, stroke and multiple sclerosis. Ohuchida discloses (Column 56, lines 7 and 9) 5-methoxy-2-propylpentanoic acid 6-methoxy-2-propylhexanoic acid compounds of instant formula (I) in which the hydroxyl groups are protected as their methyl ethers and methods for treating diseases due to reactive astrocytes such as those instantly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
6. Claim 1-16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Ohuchida et al (US 6,201,021 03-2001) in view of Rettenmeier et al (Drug Metabolism and Disposition, Metabolic Fate of Valproic Acid in the Rhesus Monkey, 1986, 14(4), pages 443-453).

Instantly claimed are compounds of formula (I), compositions thereof and a method for their use in treating neurodegenerative disease.

Ohuchida teaches (Abstract) compounds useful for the treatment of neurodegenerative disease such as Alzheimer's, stroke and multiple sclerosis.

Ohuchida teaches (Column 56, lines 7 and 9) 5-methoxy-2-propylpentanoic acid 6-methoxy-2-propylhexanoic acid compounds of instant formula (I) in which the hydroxyl groups are protected as their methyl ethers and methods for treating diseases due to reactive astrocytes such as those instantly claimed.

The difference between Ohuchida and the compounds instantly claimed is that Ohuchida does not specifically teach methoxy-2-propyloctanoic acid or the other hydroxyl and oxo intermediates.

With regard to methoxy-2-propyloctanoic acid, while Ohuchida does not specifically teach this compound, it clearly lies within the genus of compounds of formula (X) taught (Column 54, Claim 1) by Ohuchida and is part of a homologous series of

compounds that is taught by. Therefore Ohuchida can be seen to suggest this compound as well.

Further, Ohuchida teaches (Column 3, line 54- column 4, line 62) a group of compounds with similar activities that include valproic acid and 2-propyloctanoic acid. Rettenmeier, on the other hand, teaches (Page 452, Figure 7 and page 451, paragraph bridging columns 1 and 2 and 1st full paragraph, column 2) the valproic acid metabolites **9-12** and **15** all of which are compounds with $m=0$ as instantly claimed and represents the oxidation at each of the methylene groups of valproic acid. The Examiner presumes oxidation occurs at each available methylene of a compound including 2-propyloctanoic.

The compounds of Ohuchida are presumably in racemic form and are in aqueous solution. The composition claims are therefore considered to be obvious since the intended use of a composition is not considered to be further limitative.

Thus the compounds and methods as instantly claimed are inherently met in the suggested methods of Ohuchida employing valproic and 2-propyloctanoic acids.

One of ordinary skill in the art would therefore have been motivated to make the instant inventions by the teaching of Ohuchida and, for that reason, there would have been a reasonable expectation for success.

Thus the instantly claimed compounds of formula (I), compositions thereof and method of use would have been obvious to one of ordinary skill in the art.

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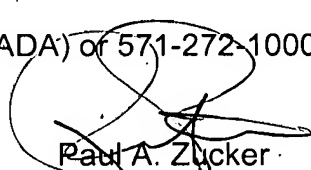
Conclusion

7. Claims 1-19 are pending. Claims 1-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 571-272-0650. The examiner can normally be reached on Monday-Friday 5:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Evonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Paul A. Zucker
Primary Examiner
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